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Award Number: DAMD17-03-1-0535

TITLE: Chemotherapy – Induced Alopecia and Symptom Distress in Younger and Older Women with Breast Cancer: Intergroup Differences and Impact on Functional Status

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REPORT DATE: August 2006

TYPE OF REPORT: Annual Summary

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
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REPORT DOCUMENTATION PAGE				Form Approved OMB No. 0704-0188	
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1. REPORT DATE (DD-MM-YYYY) 01-08-2006		2. REPORT TYPE Annual Summary		3. DATES COVERED (From - To) 7 JUL 2003 - 6 JUL 2006	
4. TITLE AND SUBTITLE Chemotherapy – Induced Alopecia and Symptom Distress in Younger and Older Women with Breast Cancer: Intergroup Differences and Impact on Functional Status				5a. CONTRACT NUMBER	
				5b. GRANT NUMBER DAMD17-03-1-0535	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Carrie Tompkins Stricker E-Mail: carrie.stricker@uphs.upenn.edu				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) University of Pennsylvania Philadelphia, PA 19104-4283				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012				10. SPONSOR/MONITOR'S ACRONYM(S)	
				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT: Purpose: The purpose of this training grant is to facilitate development of breast cancer(BC) clinical research skills, particularly related to issues relevant to older women. Scope: The research training program encompasses didactic coursework, secondary analysis, and dissertation research within the doctoral program at the School of Nursing, and intensive mentored clinical research training at the Abramson Cancer Center, both at the University of Pennsylvania. Major findings: A secondary analysis was conducted to longitudinally compare symptom distress and functional status in older (n=26) versus younger (n=163) women receiving 4-8 cycles of adjuvant BC chemotherapy. Older women trended towards greater declines in functional status from baseline to cycle 4. Age, baseline functional status, and coincident change in symptom distress together explained 55.9% of the variance in functional status change between cycle 1 and 4 (p<0.0001), with age ≥60 predicting greater declines in functional status between cycle 1 and 4. Finally, younger women's functional status scores recovered significantly more than those of older women between baseline and 1-3 months post-treatment. Progress: Secondary analysis is complete with final results presented nationally in 11/05. PhD candidacy has been achieved. All 13 required courses for the PhD have been completed, the dissertation research proposal defended, the preliminary exams defended, and ongoing dissertation data collection will be completed by 3 rd quarter 2006. As a result of work related to this training grant, the PI is a Co-Investigator on a R01 grant application submitted 6/1/06 to the National Institutes of Health (PI: Kathryn Schmitz, PhD), as well as two submitted foundation grants.					
15. SUBJECT TERMS Breast Cancer, Aging, Chemotherapy, Symptom Distress, Functional Status					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT U	b. ABSTRACT U	c. THIS PAGE U			USAMRMC
			UU	13	19b. TELEPHONE NUMBER (include area code)

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Introduction and Body

During the third year (no-cost extension) of funding for this training grant, I have fully accomplished six of eight stated objectives outlined in my approved Statement of Work. With respect to the two remaining tasks, I have made significant progress towards completion of one task (Task #3), and have obtained additional funding from the American Cancer Society to support my completion of the final task (Task #4) as well as Task #3.

1) Task 1: Participate in educational activities which extend over the entire award period.

COMPLETE. During this third year, I have continued to participated continuously in all of the outlined activities at the University of Pennsylvania (Penn), including ongoing participation in and scholarly presentations at the School of Nursing's Geroscholars seminar held by the Hartford Center for Excellence in Geriatric Nursing Education, the Rena Rowan Breast Cancer Research & Clinical Trials meeting, as well as Grand Rounds at the Abramson Cancer Center.

I have completed all 13 courses required for the PhD degree (See Appendix A). I have completed the Teaching Residency effective February 2006.

2) Task 2: Engage in a structured research residency pertaining to the conduct of clinical cancer research.

COMPLETE: See 2005 Annual Summary Report.

Task 3: Participate in subject recruitment, targeting older (>60) women with breast cancer to ensure adequate representation in UPCC 03101.

COMPLETE. See 2005 Annual Summary Report.

Task 4: Data Analysis, UPCC 03101.

COMPLETE. See 2005 Annual Summary Report.

Also, during this third funding year, I completed a secondary analysis of UPCC 03101 specifically focused on age differences in symptom experience and functional status between older and younger women undergoing adjuvant chemotherapy for early stage breast cancer. I presented final results as a paper at the annual meeting of the Gerontologic Society of America (GSA) in November 2005. This presentation included additional findings not included in the published abstract. (See "Reportable Outcomes" and Appendix B).

Task 5: Develop the design and methods of the dissertation research study.

COMPLETE. See 2005 Annual Summary Report.

Task 6: Data Collection for the Dissertation Research Study

In progress. Data collection is near completion, but is behind schedule due to factors outlined below:

- Both local (University of Pennsylvania) and Department of Defense (DOD) approval of the dissertation study protocol took longer than anticipated. Following defense of the dissertation study proposal on 6/8/06, minor changes to the protocol (required by the dissertation committee), were made and the protocol submitted to the local Institutional Review Board (IRB) approval. Initial IRB approval for the dissertation study was granted on October 1, 2005. Subsequent review by the DOD Human Subjects Review Board (HSRB) necessitated minor changes to the dissertation study protocol, outlined in a memorandum dated November 17, 2005. These changes

were incorporated, and subsequent approval of the related protocol amendment was obtained from the local IRB on November 29, 2005. Final approval was obtained from the DOD HSRB on December 22, 2005.

- Data collection for the dissertation research study began in January 2006, but completion of data collection has been delayed by difficulty recruiting a sub-sample of participants. The target sample size is 145 participants, 77 in the “younger” subgroup (<60 years old) and 68 in the “older” subgroup (≥ 60 years old). Due to the lower relative percentage of older women in the Rena Rowan Breast Cancer (Rowan) medical oncology database, the primary source of potential study participants, recruitment of older participants has been the greatest challenge. Additional funding has been obtained from the American Cancer Society (effective 8/1/06) to support continued data collection. This funding will allow recruitment of subjects from both the radiation oncology and the surgical oncology components of the Rowan database, in order to obtain a larger pool of potential participants ≥ 60 years of age. Screening of these databases is well underway, with an additional 70 potentially eligible participants (≥ 60 years) identified to date.

Table 1: Status report on data collection for the dissertation study

	Number(#) eligible subjects ¹	# Enrolled	# Enrolled, with complete data
<60 years	86	39	26
≥ 60 years	132	69	68

¹Number of potentially eligible subjects in the Rowan medical oncology database.

Task 7: Data Analysis, dissertation research study.

In progress.

- Data analysis for the dissertation research study has been delayed by slower than anticipated data collection, largely due to an inadequate initial pool of potentially eligible participants over ≥ 60 years of age (see Task 6 for further details). Data analysis will begin in September 2006.

- The Preliminary Examinations were successfully defended in July 2006, and PhD candidacy achieved.

Task 8: Prepare and submit manuscripts for publication

- See “Reportable Outcomes”.

Key Research and Training Accomplishments (7/1/05– 7/6/06)

- 1) Completed secondary data analysis for study UPCC 03101. Presented final secondary analysis results as a paper as part of a Presidential Symposium at the annual meeting of the Gerontologic Society of America (GSA), November 2005 (see Reportable Outcomes and Appendix B). Paper title: “Functional status and symptom distress in older versus younger women undergoing adjuvant breast cancer chemotherapy”.
- 2) Defended the PhD Preliminary Examinations on 7/24/06.

- 3) Submitted results of one of two PhD Preliminary Exams for paper presentation at the 59th Annual Scientific Meeting of the Gerontological Society of America (November 2006). Received notification of abstract **acceptance** July 26, 2006. (See Reportable Outcomes and Appendix B). Paper title: “Moving towards targeted physical activity interventions: Social cognitive theory and older adults”.
- 4) Began dissertation study data collection in January 2006; 94 of 145 of planned subjects (65%) have enrolled and returned complete study data.
- 5) Completed the Teaching Residency requirement for the PhD program (February 2006).
- 6) Invited content expert, Oncology Nursing Society 2005-2009 Research Agenda.
- Content area: “Late Effects of Cancer Treatment and Long-Term Survivorship Issues”.

Reportable Outcomes:

Publications:

Peer reviewed articles

Stricker, C. T. (2007, in press). Long-term consequences of breast cancer treatment: Endocrine effects. *Seminars in Oncology Nursing* 22(1).

Galantino, M. L., Brown, D., Stricker, C., & Farrar, J. T. (2006, in press). Development and Testing of a Cancer Cognition Questionnaire. *Rehabilitation Oncology*.

Book Chapters

Downs, L. H. & Stricker, C. T. (2006). Non-Hodgkins Lymphoma. In *Women and Cancer*. K. H. Dow (Ed). Philadelphia, PA: Elsevier Press.

Jacobs, L. A., Alavi, J., Demichele, A., Palmer, S., Stricker, C., & Vaughn, D. (2006, in press). Comprehensive long term follow-up: Cancer survivorship centers. In M. Feuerstein (Ed.), *Handbook of Cancer Survivorship*. Springer Publishing.

Peer-reviewed Abstracts/Presented Papers

Stricker, C. T. (2005). Functional status and symptom distress in older versus younger women undergoing adjuvant breast cancer chemotherapy. *The Gerontologist* 45(Sp. Iss. 1), p. 501. (Paper presented as part of Presidential Symposium ‘Critical Issues in Interdisciplinary Gero-Oncology Care’ at the 58th Annual Meeting of the Gerontological Society of America; Orlando, FL. November 21).

Standards, Guidelines, etc.

Berry, D. L., Champion, V., Dodd, M. et al. ... & Stricker, C. T. (2005). *Oncology Nursing Society 2005-2009 Research Agenda*. Available at the Oncology Nursing Society Website: <http://www.ons.org/research/information/agenda.shtml>.

Monographs

Stricker, C. T. (2005). Overview of breast cancer therapy & treatment of metastatic disease. In *The Breast Cancer Panel: A case-based discussion on the use of targeted therapies for primary and metastatic disease*. Miami, FL: Institute for Medical Education and Research. (CEU monograph).

Stricker, C. T. (2005). Chemotherapy-induced nausea and vomiting. In *Who wants to be a supportive care expert*. Miami, FL: Institute for Medical Education and Research. (CEU monograph).

Lay Publications

Stricker, C. T. (2005). Managing Long-Term Side Effects of Breast Cancer Treatment. *Insight: Living Beyond Breast Cancer's Newsletter*, Fall 2005, pp. 1-2, 10.

Presentations:

National and International

- 2006 "Breast Cancer: A Case-Based Discussion on the Use of Targeted Therapies"
- Continuing Education Symposium (Coordinator & Speaker)
Oncology Nursing Society 31st Annual Congress, Boston, MA; May 4.
- 2006 "Advanced Practice Nursing & Cancer Survivorship"
3rd Annual Scripps Oncology Nursing Advanced Practice Conference: Innovation through Practice. San Diego, CA; 4/2.
- 2005 "Symptom Management and Sexuality Issues in Women with Breast Cancer"
- Parallel Session, Breast Cancer in the Elderly
International Society of Geriatric Oncology (SIOG); Geneva, Switzerland; September 30
- 2005 "A Cancer Survivorship Multidisciplinary Clinical and Research Program"
- Discussion Session, American Journal of Nursing State of the Science Conference:
Long Term Sequelae of Cancer and Cancer Treatment; Philadelphia, PA, July 16.

Regional

- 2005 "Exercise Programs for Individuals with Cancer: A Review of the Evidence"
Tumor Board, Lehigh Valley Cancer Center; Allentown, PA. November 3.

Research opportunities:

1) Invited Co-Investigator on the international study "Nausea and vomiting after chemotherapy: validation of a short clinical scale", funded by an investigator-initiated studies grant from Merck & Co, Inc. (PI: Alex Molassiotis, PhD, RN; University of Manchester), and supported by the Multinational Association of Supportive Care in Cancer.

Funding awarded:

Stricker, C.T. (\$15,000)

American Cancer Society, Doctoral Scholarship in Cancer Nursing
8/01/06-7/31/07 (Non-competing renewal of FY '06 award)

"Physical Activity Determinants and Behavior in Older Breast Cancer Survivors"

Funding applications:

Based on the work supported by this training grant, I am a Co-Investigator on several related proposals which have been submitted for both federal and foundation grant funding. All grants are currently under review. These include:

- 1) “Physical functional status in breast cancer survivors: understanding long term effects of treatment” (PI: Kathryn Schmitz, PhD). Submitted June 1, 2006 to the National Cancer Institute under the R01 mechanism.
- 2) “Physical functional status in breast cancer survivors: effects of treatment” (PI: Kathryn Schmitz, PhD). Submitted June 30, 2006 to the Oncology Nursing Society for the ONS Foundation Breast Cancer Research Grant - (RE22) RFA. Also submitted June 30, 2006 to the Lance Armstrong Foundation Request for Grant Proposals: Issues of Cancer Survivorship – General Research Awards mechanism.

Conclusions:

Major progress has been made in year three towards achieving the objectives of the Clinical Research Nurse Award training grant, with most tasks completed. The inability to complete the remaining two tasks (data collection and analysis for the dissertation research study) reflects overambitious objectives for this training grant. Additional funding has been secured from the American Cancer Society to allow completion of these remaining tasks, and graduation with the Doctor of Philosophy (PhD) degree is anticipated in May 2006.

Although data collection for the dissertation study is still underway, several other research and training projects have been fully completed during the term of this two-year grant and one-year no-cost extension. Secondary analysis of a separate study (UPCC 03101) is complete, and findings were presented orally at the Gerontological Society of America in November 2005 (see Appendix B). The preliminary examinations were successfully defended in July 2006, and a related paper will be presented at the Gerontological Society of America in November 2006. All requirements for the PhD degree have been completed except for the final dissertation defense. Thirteen required courses have been completed (See Appendix A), the Qualifying Examination and Preliminary Examinations defended, the Teaching and Research Residencies completed, and data collection for the dissertation research study is well underway.

This training grant has afforded the Principal Investigator (PI) the opportunity to engage in independent and collaborative research projects that not only have enhanced her clinical research skills, but have also led to additional collaborative research opportunities. As a direct result of preliminary work on functional status in women diagnosed with breast cancer that was undertaken as part of this grant, the PI is a Co-Investigator on several applications for funding currently under review by the National Cancer Institute and two private foundations. She is also currently collaborating on an international research project supported by the Multinational Association of Supportive Care in Cancer. The time, resources, and mentorship afforded by this training grant were essential to securing these opportunities.

APPENDIX A: Doctoral Coursework

Completed during the FY2006 funding period

- Nursing 840: Proseminar in Advanced Quantitative Designs and Methods for Nursing and Health Research

Completed during the FY2005 funding period

- Epidemiology 542: Measurement of Health in Epidemiology
- Nursing 900: Functional Adaptation to Chronic Illness in Older Adults (Directed Study)
- Nursing 900: Exercise Physiology & Physical Activity Measurement: Applications to Clinical Research in Older Adults with Cancer (Directed Study).
- Sociology 536: Quantitative Methods in Sociology II (Statistics II).

Completed during the FY2004 funding period

- Nursing 753: Evolving Nursing Science
- Nursing 813: Qualitative Paradigm Empirical Nursing Research
- Nursing 816: Health Status, Functional Status, & Quality of Life
- Nursing 800: Dissertation Seminar
- Public Health Studies 504: Behavioral and Social Sciences in Public Health

Completed prior to funding

- Nursing 750: Inquiry and Nursing
- Nursing 754: Quantitative Research Design and Methods
- Sociology 535: Quantitative Methods in Sociology (Statistics I)

APPENDIX B:
Published Research Abstracts

Final Secondary Analysis Results:

Stricker, C. T. (2005). Functional status and symptom distress in older versus younger women undergoing adjuvant breast cancer chemotherapy. *The Gerontologist* 45(Sp. Iss. 1), 501.

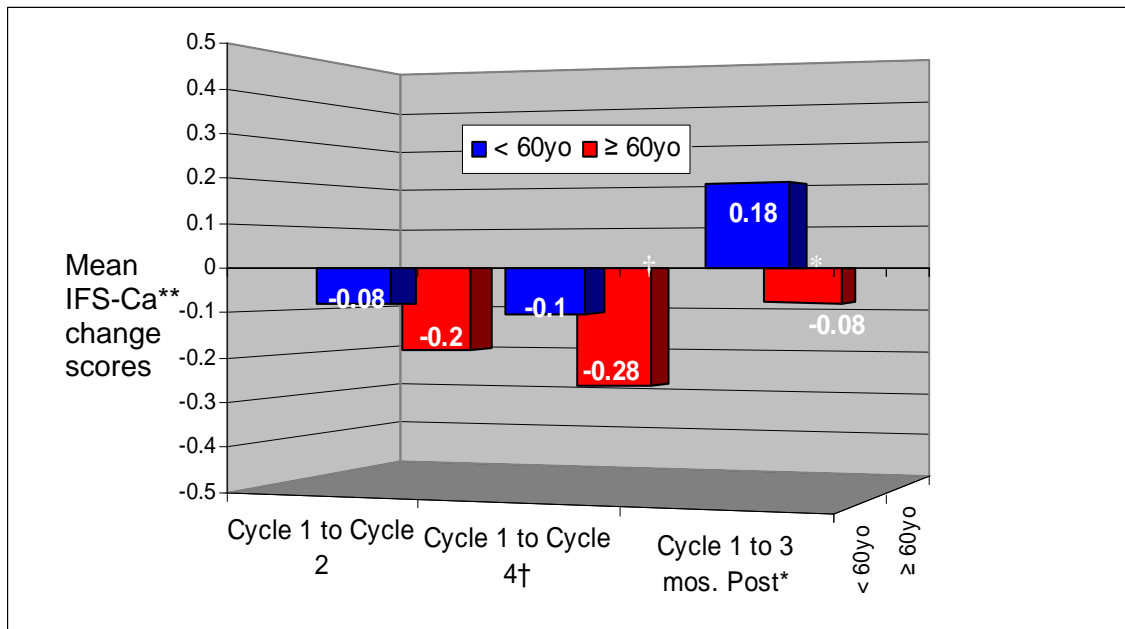
Background: Women 65 and older constitute over 50% of new breast cancer cases in the United States, yet are significantly under-represented in clinical cancer research. The number of older women receiving adjuvant chemotherapy for early stage breast cancer is growing, yet little is known about how these women's unique experiences of symptom distress and functional status throughout chemotherapy compare to those of younger women. Recent studies of women receiving heterogeneous treatments have yielded conflicting results. Furthermore, predictors of symptom distress and functional status are not well understood in this population. The purpose of this study is to compare symptom distress and functional status in older versus younger women receiving adjuvant breast cancer chemotherapy, and to identify predictors of functional status changes in this population. **Methods:** A secondary analysis was performed on a dataset from a longitudinal study examining relationships between symptom distress, anemia, and functional status in women during and following anthracycline-based adjuvant chemotherapy for early stage breast cancer. Symptom distress (Symptom Experience Scale) was measured at baseline before chemotherapy, on Day 1 of cycles 2 and 4, on Day 8 of cycle 1, and 3 months following the completion of chemotherapy. Hemoglobin (g/dL) and functional status (Inventory of Functional Status-Cancer) were measured concurrently, except on Day 8. Baseline demographic and treatment variables included age, marital status, race, stage, type of surgery, and days since surgery. Change scores were calculated by subtracting the score for a variable at one time point from its corresponding score at an earlier time point. **Results:** Data from 189 women (mean age=48.8 years, range 25-77) were analyzed. Older women were defined as those 60 years or older (n=26), and younger women, less than 60 years (n=163). In each group, functional status and hemoglobin declined significantly from baseline to cycle 4, and returned to or above baseline by 3 months following chemotherapy. Symptom distress exhibited the reverse pattern. Compared to younger women, older women experienced a trend towards greater decline in functional status from baseline to cycle 4, despite lack of significant differences in functional status at any one time point. Older women had significantly lower symptom distress and rises in symptom distress during the first week following chemotherapy than did younger women, but there were no significant differences in symptom distress at any other time point. Age, race, baseline functional status, and coincident change in symptom distress together explained 55.9% of the variance in change in functional status between cycle 1 and 4 ($p<0.0001$). No other demographic/treatment variables explained differences in functional status. **Conclusions:** Older women represent the largest population of women with breast cancer in the United States, and are at risk for greater declines in functional status during adjuvant chemotherapy. Minimizing symptom distress may help to prevent functional status declines in these women.

Additional findings presented at the meeting, but not published in *The Gerontologist*:

In order to compare changes in functional status over time between older and younger women, change scores were calculated between cycle 1 (baseline) and cycle 4, as well as cycle 1 and a follow-up timepoint occurring 1 to 3 months following chemotherapy. A non-significant trend was observed for change in functional status between baseline and cycle 4 of chemotherapy, with older women experiencing numerically greater declines in functional status when compared to their younger counterparts. A statistically significance difference between older and younger women was observed for the change in functional status between baseline and

1 to 3 months following chemotherapy. Not only do older women not recover beyond their baseline post-surgery functional status at a timepoint 3 months post-chemotherapy, but their recovery of functional status between these two timepoints is significantly less than that of younger women (See Figure 1).

Figure 1: Changes in functional status over time by age group



* $p = 0.044$ ($t = 2.037$) for difference between age groups

† $p = 0.137$, trend for difference between age groups

** IFS-Ca = Inventory of Functional Status – Cancer. Change scores were calculated by subtracting total IFS-Ca scores of the later timepoint from those of the earlier timepoint.

Preliminary exam findings:

Stricker, C. T. (2006). Moving towards targeted physical activity interventions: Social cognitive theory and older adults. (Paper to be presented at the 59th Annual Meeting of the Gerontological Society of America; Dallas, TX; November. Abstract to be published in *The Gerontologist*).

Physical activity (PA) plays a major role in the health and functioning of older adults, yet few older adults engage in recommended levels of PA. Social cognitive theory (SCT) has proven valuable for understanding PA. Based on a careful integrative review of SCT, new approaches to interventions aimed at physical activity in older adults deserve attention. This integrative review analyzes results from 18 studies that examine SCT constructs as predictors of PA in older adults, with the goal of identifying implications for future intervention research. The utility of SCT in this setting is strongly supported, as SCT constructs and their antecedents explained a moderate to large (29 to 67%) variance in PA. Self-efficacy (SE) and outcome expectations (OE), two core SCT constructs, consistently influence PA. Variables such as social support for exercise (SSE), the environment, exercise enjoyment, and social modeling have positive effects but have undergone limited investigation, as have relationships between these and other variables. In order to design effective PA interventions for older adults, more comprehensive and sophisticated models of SCT constructs must first be examined. Such study will allow interventions to be targeted to individuals based on profiles of relevant characteristics, such as high SE and a facilitative environment but low SSE. In addition, dedicated study of older women, minority groups, and chronically ill older adults is greatly needed. Together, these strategies ultimately have the potential to increase PA in older adults, a population particularly vulnerable to the influence of inactivity.